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RADIUM

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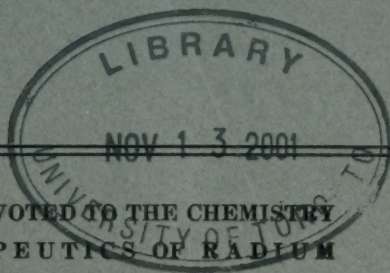
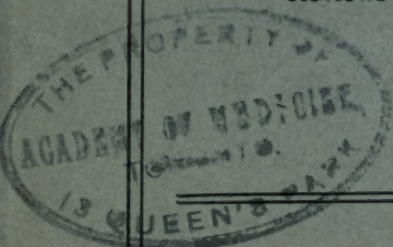
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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY
PHYSICS AND THERAPEUTICS OF RADIUM
AND RADIO-ACTIVE SUBSTANCES

RADIUM

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Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D.
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VOL. VII.

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RADIUM IN THE TREATMENT OF CARCINOMA OF THE CERVIX UTERI*

C. JEFF MILLER, M.D., F.A.C.S.,

NEW ORLEANS, LOUISIANA.

It is unfortunate that so much labor and time are required in attesting the true valuation of a therapeutic agent. Chemists, physicists, physiologist, and clinicians must combine the results of their many labors, and even after their work is completed it is often difficult to make the final deductions properly; to eliminate faulty methods and premature claims of over-enthusiastic pioneer investigators.

The investigation of so-called cancer cures is especially difficult because of the length of time required to check the ultimate results.

Radium has proved no exception to the rule; in fact its novel chemical qualities, its absolutely original physical phenomena and the premature claims as to its wonderful therapeutic properties have doubly confused rather than clarified our knowledge of its actual virtues. It has been used about ten years in the treatment of disease, during which time it has been lauded in the highest terms; abandoned as useless by some, and denounced without trial by many. The first seven years of its use produced only scattering reports. It was in the experimental stage and available for study by only a few clinicians, and it may be said that the statistics of real value have been produced within the past three years, since the methods of application and screening have been better understood, and a larger supply of the element has been available.

*Surgery, Gynecology and Obstetrics, XXII, 437-441, April, 1916. Presented in the symposium on "Cancer of the Uterus," at the meeting of the Chicago Gynecological Society, December 17, 1915.

From the numerous clinical data now collected, certain well established facts may be gathered. First among these facts should be mentioned the remarkable influence of radium over uterine bleeding associated with the metropathies, fibromata, and carcinomata. This faculty alone establishes it as an agent of the first rank in the treatment of probably the commonest affection for which the gynecologist is consulted.

There is no longer the slightest doubt that it exerts a powerful influence over cancer-cells. This influence is not the result of cauterization, as many pathologists would have us believe, nor is it because of any selective action on cancer-cells, but rather its effect on all cell life. Its effect is well described by Burnam, who states that "it can be assumed that radiation deleteriously affects all living tissue, but under this injurious influence the normal tissues are preserved because the fluids and the protective agencies of the body are all constructed to help the normal tissues, and that the pathologic tissues disappear because, weakened by radiation, they are unable to withstand the normal protective mechanism of the body. This readily explains why a similar growth in different individuals will react differently or not at all to radiation; why slight radiation will effect marvelous changes in one case and show just the opposite changes in another. It must also be borne in mind that certain normal tissues are more resistant than others and that the latent period of radiation may be influenced by all of the above-named factors and promptly points to numerous problems yet to be solved by radiophysicists. Whether the solution of these problems depends upon earlier treatment, larger dosage, more efficient screening, or by combining radiation with operation or other therapeutic agents, remains for the future to solve."

There is another point which must be kept constantly in mind by the clinician; viz., his duty and obligations to the already proved principles of the surgical treatment of cancer.

Surgery is the only treatment so far known that offers a permanent cure for cancer in the early stage of the disease. No discussion which might detract from the high esteem in which surgery is held should be allowed to filter out to the inexperienced practitioner and particularly to the public at large. Until something more satisfactory than surgery is positively proved, we must unite in the common cause of educating the public to the importance of early surgical treatment, remaining in the meantime in a receptive attitude toward the efforts of investigators to reach the common goal by other avenues. We must agree that we have about reached the limitations of operative technique in cancer eradication. No one may venture farther than the present established technique of breast amputation or radical hysterectomy. If we increase our percentage of ultimate cures it will be by earlier operation or by combining other therapeutic agents with surgery.

The most promising agent so far known is radiation, either by special X-ray apparatus or radium. Both agents are scarcely beyond their infancy and their wonderful properties seem to be manifold and lead into divers ramifications.

It is not difficult to define my attitude toward radiumtherapy after the above remarks. So far I have employed it solely as an adjunct to surgery. I have not been satisfied with the results of radical operation, not to mention the 60 to 70 per cent. who come so late for treatment

that even palliative measures are often useless and burdensome to the doomed patient.

As my experience with radical operation increased, the percentage of cases in which I advised it gradually decreased. I no longer recommend it in the so-called borderline cases, believing that such formidable treatment, with its primary fatalities and subsequent morbidity, does not give sufficient returns for the risk incurred. It was with the idea of increasing the permanent results obtained by surgery by the combination with radium, the conversion of inoperable into operable cases, and last but not least the amelioration of the suffering of the hopeless cases, that I determined to try radium.

I regret that I can offer as yet no statistics that might show that my operative results have been improved by the use of radium prior and subsequent to operation. Such conclusions must necessarily be based upon a large series of definitely classified cases by the same operator doing the same type of operation and following the cases for a longer period than any one has yet been able to extend their observations. Prophylactic raying after operations is now fairly well established on a rational basis. The only statistics at my convenience bearing on this point are those of Gauss, who reported that of 21 operated upon and rayed, 20 had remained free from recurrence up to six years after operation, while their previous experience showed that in 60 per cent. of cases operated upon without radiologic treatment the disease showed evidence of recurrence within one year.

I also regret that I cannot produce practical personal evidence that preliminary application of radium will convert inoperable into operable cases. Improvement has been so gratifying in four of my cases that I have repeatedly urged hysterectomy, but notwithstanding my strongest arguments, three positively declined, stating that they had improved so satisfactorily that they were willing to assume the risk. The fourth has agreed to submit to operation within a few weeks. I may add that many good authorities differ as to whether or not advanced cases become operable under radium therapy. Whether or not the accompanying parametrial involvement which disappears under radiation is of malignant or inflammatory origin cannot be determined without operation and offers another serious difficulty in diagnosis. There is no doubt that radium applications prior to operation add some difficulties to the operative technique. The widespread connective-tissue changes would necessarily make the usual dissection exceedingly tedious and must be taken into consideration when it is decided to operate after radium treatment.

It is the tendency at present to operate on more of these cases than formerly, so it will be only a matter of time before the value of the combined treatment is fully known.

The results I shall present are derived from the application of radium in 20 cases of inoperable cancer of the cervix uteri and recurrent cancer following hysterectomy that have come under observation since May, 1914. All have been followed up to December 1, 1915. The list is small and the length of time that has elapsed too short to permit of practical deductions except as to the primary results of radiumtherapy. It permits me, however, to state most emphatically that radium is a great boon to patients suffering from inoperable and recurrent cancer of the cervix uteri. I have seen large inoperable carcinomata fixed in the pelvis entirely disappear within a month and the patient's general condition correspondingly improve. Bleeding was almost invariably controlled

within two weeks and the foul discharge disappeared almost as rapidly. Even in cases in which the local process did not respond the bleeding was checked, the discharge changed in character, the pain usually decreased and the general condition improved for a short period. Fifteen inoperable cases were treated solely with radium. They were far advanced, showed the usual cachexia, and several were not good risks even for simple cauterization under anesthesia. Four have died and two are slowly succumbing to the disease. Five are apparently free subjectively and objectively of disease. Among the five who are apparently well are two of the earliest cases and the others were treated about nine months ago. The primary results were almost uniformly good when the condition at the time of treatment is considered).

Four cases did not respond to treatment. They were far advanced, the vagina, bladder, and rectum being involved. Bleeding was checked and the pain reduced but they gradually lost ground and died within two months.

The first case in this series was treated in May, 1914. She writes November 20, 1915, that she had a slight hæmorrhage in March, 1915, but it lasted only a day. She has been comfortable since but has lost some weight. Four in the series showed evidence of returning trouble about 6 months after treatment, but responded to further applications. It is too soon to tell how long they will remain free from symptoms.

It is interesting to observe the remarkable deodorizing action of radium. Sepsis is the commonest complication of advanced cervical cancer and the attending foul discharge is the most disagreeable feature both to the patient and her attendants. Ten days after radium applications the odor begins to disappear and the temperature, if present, usually subsides. This effect alone has prompted several patients to state that the treatment was worth while, whatever the final results might be.

The relief of pain is usually as marked as the control of discharges. Pain is usually due to the septic complication and consequently subsides as the local process improves. The subsidence of pain, however, does not depend entirely upon this factor, as I have seen patients abandon opiates within 24 hours after the first application.

CASES CAUTERIZED PREVIOUS TO RADIUM TREATMENT.

Six cases has been excochleated and burned one to five months prior to radium treatment. In every instance the disease was rapidly reappearing when radium was first applied. The first case was treated in May, 1914. She was cachectic, suffered intensely, and had an exceedingly offensive discharge. The bladder was involved, the rectal wall was infiltrated and the remaining parametrial structures fixed. She improved rapidly, gained 17 pounds in weight, and the local process completely disappeared. She remained well until October, 1915, then died after a brief illness. Her physician stated that no evidence of trouble could be found in the vaginal vault. Since she had excruciating pain in her left hip for two weeks before her death, it is to be believed that she died of metastases remote from the vaginal vault. Three of these cases are apparently free from disease twelve months after treatment.

Just at this point it is apropos to discuss whether or not it is better to burn or use the curette on sloughing masses before applying radium.

My experience leads me to believe that it is not the best mode of procedure. I am positive that it required a longer time to check the

local symptoms and the subsequent histories do not show that they remained well any longer for having had the preliminary cauterization. Preliminary cauterization requires anaesthesia and is attended by no little discomfort and certainly retards the primary effects of radiation. My experience is corroborated by others, especially Burnam, who recently stated that he no longer cauterized and curetted sloughing masses as a preliminary measure.

RECURRENT CARCINOMA AFTER HYSTERECTOMY.

I have applied radium to malignant areas reappearing in the vaginal vault after hysterectomy in 6 cases. These cases are utterly hopeless from a surgical standpoint and unfortunately are much less amenable to radium-therapy than primary processes. In four cases the growth promptly responded to treatment but the results cannot yet be known owing to the short period elapsed since the applications were made. The first case presented a fungus bleeding mass in the vault two years after I had performed hysterectomy. Radium was used in December, 1914. She was entirely free of local symptoms when examined December 1, 1915, and her general health is excellent. Two other cases are apparently well six months after treatment. In one case the mass disappeared, but the patient died soon after from an infected kidney.

In another instance local masses have responded twice within the past year to applications, but her general condition is gradually waning.

I have related in a general way these personal experiences to show just what my results with radium have been so far. As you will see they do not prove that radium will cure cancer, for the most favorable cases have not been followed yet two years. They prove conclusively to my mind, however, that cancer of the cervix is profoundly influenced by radiation in cases that are hopeless surgically and that the results were accomplished with a minimum of discomfort to the patients. I may further add that the results so far are superior to any other method I have used in similar cases.

The primary result is often beyond the hopes of its most enthusiastic supporters. Bedridden sufferers have been given a new lease on life and some have been improved to the extent that surgery might be beneficial when it was originally useless. The remarkable primary results caused many early workers to report cures which were unfortunately only temporary symptomatic cures. The same test of time must be applied as in surgical statistics before they are transferred to the cured column.

One point in favor of radium which should not be overlooked in the final analysis is that the present statistics will be based upon material that has passed beyond surgical relief before radium is used. If radiation can show even a fair percentage of cures at the end of five years, its usefulness will be fully established in a class of cases not amenable to any other form of treatment. The chief point of interest after all is the duration of radium treatment. The only recent available statistics that might throw light on this phase of the subject are those of Kelly and Burnam. Schmitz has also published some extremely interesting figures, but like my own, the cases can be followed only since April, 1914.

The statistics of Kelly and Burnam probably contain more cases observed over a longer period than any other single clinic can show at present. They report 57 clinical cures; 35 cases of original inoperable cancer of the cervix uteri and vagina, and 18 cases of originally in-

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operable recurrent cancer. One cure has lasted 6 years; 3 for over 4 years; 4 for over 3 years; 5 for over 2 years; 29 for over 1 year, and 15 for 6 months. If this list is again summarized two years hence, we may begin to learn something of the ultimate results.

Cheron and Rubens-Duval's statistics approach approximately those of Kelly and Burnam in number and length of time observed and practically coincide with the latter's figures.

TECHNIQUE.

There still exists a wide difference of opinion as to the proper usage of radium in treating uterine cancer. Some believe that the problem is solved when sufficient radium can be made available to give massive doses hitherto impossible owing to the scarcity of the agent.

Schauta, Kelly and Burnam, Kroenig, Wickham, and others believe in massive dosage while other equally well-known observers believe that smaller amounts applied for a longer period will accomplish the same results.

What the final conclusions will be remains to be seen, but it is generally agreed that less than 50 milligrams of the *radium element* should not be employed, lest the growth be stimulated instead of causing the necessary necrosis.

Pinch, who has large quantities of radium at his disposal, finally decided upon a dosage of 50 to 100 milligrams. Schmitz used uniformly 50 milligrams giving 6 to 8 séances of from 10 to 12 hours. The course is followed by an intermission of three weeks. If examined there reveals an apparent cure, two or three applications of 500 or 600 milligram hours of radium element is given every second or third day, followed by another interval of three weeks.

This has been practically my plan with the exception that I use from 75 to 85 milligrams of the radium element and endeavor to give from 3,000 to 5,000 milligram hours within a week or ten days. One month later further applications are made according to the indications.

No one can doubt that cancer of the cervix can be entirely eradicated by radium. Unfortunately it is not the cervix *per se* that controls the ultimate termination; the outlying cancer areas in the broad ligaments and the glandular metastases really control the situation. If the penetrative powers of radium can be made to reach the outposts of the disease, its value will be inestimable.

Bumm's widely quoted experiments which showed that the limit of the gamma-ray efficiency (in tissue) was about 4 cm. is now very correctly questioned by Burnam, who states that it is possible to radiate any distance by proper distribution of the applicators, all of which goes to show that the seemingly insurmountable obstacles are being overcome as experience increases. To prove that cancer can be anatomically cured will be much more difficult than any phase of the work so far accomplished. It will require not only long years of observation, but it will require as well a microscopical study of serial sections of outlying tissues removed at subsequent operations and at post-mortem findings. This is a task stupendous in itself and can only be solved in the manner recently illustrated by Schmitz, Cheron and Rubens-Duval, and others.

The scope of this paper does not permit of much more than a statement of my personal experience. I cannot offer any general conclusions other than to say that radium has a wide field of usefulness, the real value of which can be estimated only after painstaking collective studies. It has no field absolutely to itself but is merely a therapeutic agent which should be used in common with other well-established methods of treatment.

CONTRIBUTION ON THE THERAPEUTIC VALUE OF THE INTRAVENOUS INJECTION OF SOLUBLE RADIUM SALTS IN THE TREATMENT OF PERNICIOUS ANAEMIA AND LEUKAEMIA.

BY FREDERICK PROESCHER, M.D.

EPICRISIS OF CASES.

Case 1. is a *morbus* Biermer where the megaloblastosis was absent during the entire course of the disease. Nucleated red cells were seldom found in spite of the numerous examinations. The macro, micro and poikilocytosis as well as the hyperchromasia with a color index 1.2 were pronounced, and the relative lymphocytosis strengthened the diagnosis of essential pernicious anaemia. The anisocytosis of the red cells without the accompanying hyperchromasia would rather have suggested a diagnosis of secondary anaemia.

After the diagnosis was established the case was treated for a little over four weeks with subcutaneous injections of cacodylate of soda. In spite of the rigorous arsenic treatment on January 8, 1913 the red cells were considerably decreased from 2,250,000, which the first examination on December 1, 1912 showed, to 1,575,000, the color index was increased to 1.4. I suggested to the attending physician that he abandon the cacodylate treatment and advocated the subcutaneous arsacetin treatment in the manner described above. After the arsacetin injection the red cells and hemoglobin increased gradually. April 20, 1913 the red cells were increased to 4,500,000 hemoglobin 11.96 gm. (85.4%); color index .9, while the leucocyte count showed a decrease to 1,000. May 25, 1913, twenty days after the last arsacetin injection the red cells were increased to 4,600,000, the hemoglobin to 16.76 gm. (119.7%); and the color index to 1.3.

If we summarize the effect of almost six months arsenic treatment we see that under the cacodylate treatment the red cells and hemoglobin were markedly decreased. The color index increased to 1.4. If this was due to the cacodylate or caused by the still progressive hemolytic process, not influenced by the cacodylate, is open to question. Whether the arsacetin really influenced the morbid process of if the remission, independently of the treatment set in, is impossible to decide. The numerical increase of the red cells in spite of the rigorous arsenic treatment compared with the initial findings is not very considerable, but the most striking increase was manifested in the hemoglobin content. The microscopical aspect of the stained blood films still showed a slight macro and microcytosis and also a few poikilocytes. The differential count did not show any material changes as a marked lymphocytosis prevailed throughout the entire arsenic treatment. The only result of the arsenic treatment, if we can attribute any to it, is an increase in red cells and hemoglobin. The red cell aspect still showed degenerative signs and the leucocyte picture was not influenced at all.

May 25, 1913—The patient received the first intravenous injection of 250 micrograms radium element in the form of radium bromide. The next three days following the radium injection the red cells were decreased 550,000, the hemoglobin content was also slightly lowered, while the color index remained almost the same. The leucocytes showed

an increase from 5,620 to 7,750. May 31, 1913, the red cells were increased again to 4,550,000 the hemoglobin 117.5%, the leucocytes increased to 9,250. The differential count showed a decided relative increase of the polynuclear neutrophiles from 44.46% to 56.49%. The monocytes also were increased from 1.66% to 9.64%. June 3, 1913, the red cells reached their maximum and showed an increase to 6,050,000, the hemoglobin increased to 153.1% (21.44gm.) while the color index was 1.2 and the leucocytes had decreased to 6,500. The differential count showed a decrease of the polynuclear neutrophiles to 48.00%. The red cell aspect during the above described period showed a slight poikilocytosis while the macro and microcytosis had almost disappeared. The hypochromasia of the red cells was unchanged. From June 10th until October 28, 1913 the red cells showed as a maximum 5,000,000 and were lowered to a minimum of 3,200,000 (October 28, 1913). The hemoglobin decreased from 117.4% to 98.2%. The color index during this period was once found to be below 1, *i.e.* on July 5, 1913 color index was 0.9.

The absolute leucocyte count, with the exception of June 10, 1913, when it reached 17,500; (the highest count noticed during the entire period of our observation) showed almost normal values. The differential count showed a continuous relative increase of the neutrophile leucocytes from 46.00% to 51.56%. Anisocytosis, poikilocytosis and hyperchromasia of the red cells were present in a slight degree. On account of the decided decrease of the red cells the patient received from November 22, 1913 to December 22, 1913, another series of injections of arsacetin. The blood examination on March 1, 1914, showed that the red cells had increased to 4,250,000, while the hemoglobin was further reduced from 98.2% to 94%, color index 1.1, leucocytes 8,250. Polynuclear neutrophiles were relatively increased to 55.80%. A period of six months elapsed until the patient presented himself for a further blood examination. June 8, 1914 patient came in a very debilitated condition, he was weak and markedly anaemic. The blood count on the same day showed that the red cells had decreased to 1,376,000, the hemoglobin to 34.1%, color index 1.3, leucocytes 7,000. Polynuclear neutrophiles were relatively increased to 71.53%; anisocytosis, poikilocytosis and hyperchromasia of red cells were all pronounced. He received from June 10, 1914 to August 11, 1914, 8 grams of arsacetin. Repeated blood examinations during this time did not show any appreciable effect upon the red cells and hemoglobin. The red cells were only slightly increased to 1,520,000 (July 10, 1914). The hemoglobin 36.3%, color index between 1 and 1.3, there was a pronounced leukopenia with the polynuclear neutrophiles relatively decreasing. On July 10, 1914, 250 micrograms radium element were injected. During the next three weeks following the radium injection no influence on the red count was noticed. Hemoglobin somewhat increased (36.3% to 47%). Pronounced hyperchromasia, color index 1.4 to 1.7, leukopenia. Relative increase in polynuclear neutrophiles (68.50%). Anisocytosis and poikilocytosis pronounced. 100 micrograms radium element injected on August 11, 1914. On August 18, 1914 a slight increase in the red cells 1,656,000, hemoglobin 38.4%, color index 1.1. Very pronounced leukopenia (2750). During the next seven months a further continuous decrease of the red cells was noted. On March 9, 1915 the red cells were decreased to 1,084,000, hemoglobin 40%, color index 1.8, leucocytes 4,100.

If we summarize the influence of the radium upon the blood picture we come to the following conclusions:

After a latent period of approximately six or eight days during which time the red cell count was somewhat lowered, a marked increase of the red cells and the hemoglobin was noted. During the next six weeks observation the red cells remained at almost their normal number and once the proportion of the hemoglobin and red cells, as indicated by the color index (0.9), was found normal. We can safely say that such an increase is not due to a spontaneous remission, but must be attributed to the influence of the radium upon the erythrocytes, but this extraordinary increase was only temporary as a few days later the red cells decreased to subnormal while the hemoglobin, which was also considerably lowered, was still abnormally high as the color index indicated. It is striking that during this blood crisis only a few nucleated red cells were found. The microscopical aspect of the stained blood films still exhibited a slight degree of anisocytosis and the hyperchromasia was pronounced.

How long the approximately normal red cell picture was retained cannot be stated, since no blood examination was made during the next three months. July 19 to October 28, 1913 the general condition of the patient was good and he was able to attend fully to his work. A blood examination at the end of October, 1914, showed that the red cells were considerably decreased with a high color index while the hemoglobin was about normal. Another series of arsacetin injections increased the red cells again, while the hemoglobin still declined. Whether this remission was due to the arsacetin or was spontaneous in its nature, is difficult to decide.

On January 3, 1914 the patient was in a fairly good condition, still able to work. Unfortunately during the next six months the patient did not return for further blood examination and we did not see the patient before June 9, 1914 in an extremely weak and anaemic condition. Further injection of arsacetin and radium were without any influence upon the blood picture. In spite of the extremely low red cell count the patient lived almost a year, dying August 19, 1915, of exhaustion.

Case No. 2.—This case illustrated a kryptogenetic infection (generalized infectious lymphadenitis of unknown origin) with a pernicious anaemic blood picture. The absolute count showed a very marked reduction of the red cells and hemoglobin with a color index 1.2, no leukopenia. Differential count showed a relative lymphocytosis and a slight "reizungsmvelocytosis."

The microscopical aspect of the stained blood films showed anisocytosis, hypo and hyperchromasia and reduction of the blood platelets and many erythroblasts and giantoblasts. The patient was treated with radium only and received no other medication. He received 400 micrograms radium element intravenously (April 14, 1914). During the next four weeks the red cells and hemoglobin showed a steady increase, showing on April 13, 1914 an increase from 1,376,000 to 2,800,000 and the hemoglobin from 27.7% (3.38 gm.) to 70.3% (9.84 gm.), while the color index was still above 1. The leucocytes were first lowered and at the end of four weeks increased. Another injection of 100 micrograms on May 13, 1914 showed two days later a still somewhat higher red count (3,152,000) while the hemoglobin was a little lowered. The color index was 1. The relative leucocyte count showed the following: The poly-

nuclear neutrophiles were slowly increased from 13.89% (April 14, 1914) to 36.5% (May 1, 1914) but decreased again to 21.75%. The polynuclear eosinophiles as well as the lymphocytes showed only a slight variation. The neutrophiles, myelocytes and myeloblasts disappeared entirely. The leucoblasts and monocytes were markedly diminished. The erythroblasts and giantoblasts showed no marked fluctuation. The microscopical aspect of the red cells showed at the end of the four weeks observation a slight anisocytosis, hyperchromasia and polychromasia of the red cells.

The rapid and steady increase of the red cells was without doubt supported by the radium. Of course a spontaneous remission which may have in time corresponded with the radium treatment cannot be entirely excluded.

It is to be regretted that no further observation of this case was possible. The attending physician, Dr. Pettit, reports the patient to be in fairly good condition and working, but unwilling to present himself for further examination, thereby leaving this interesting case incomplete.

Case No. 3.—This leukaemia case was the first one treated with massive doses of radium element intravenously. He received 2,700 micrograms equal to 7,290,000 mache units in 13 months. The first blood count on July 1, 1913 showed 4,087,500 red cells, 12.84 gm. hemoglobin (91.7%), color index 1.1, leucocytes 222,500. The stained blood films showed a mixed cell leukaemia of a myeloid-myeloblastic type.

The patient received from July 1st to July 7, 1913, 400 micrograms radium element, in 100 microgram doses, given every two days. Twenty-four hours after the first injection the red cells showed an increase of 1,637,500. The hemoglobin was only slightly increased (2.3%) while the white cells were increased to 272,500. After the second injection the red cells were lowered about 756,000 while the hemoglobin was still further increased to 14.36 gm. (102.6%), and the leucocytes increased to 280,000. After the third injection the red cells and the hemoglobin remained almost the same while the white cells were lowered to 245,000. After the fourth injection the red cells showed a very slight decrease of about 15,000, while the hemoglobin was lowered from 13.6 gm. (99.7%) to 8.96 gm. (64%). The white cells showed a slight increase from 245,000 to 265,000, the color index which was before the radium injection about 1.1 was lowered to .6. Four days later (July 12th), after 400 micrograms radium element had been given, the red cells increased to 8,350,000, the hemoglobin to 15.24 gm. (108.9%), color index .6, while the white cells were 231,200. The red cells in two days showed an increase of 4,262,500. It is remarkable that no abnormal increase of nucleated red cells was noticed. Between July 5, 1913 and August 17, 1913 the red cells slowly decreased from 8,350,000 to 5,300,000, the hemoglobin was also lowered from 15.24 gm. (108.9%) to 13.44 gm. (96%). The white cells showed a steady increase from 242,500 to 350,000. On December 20, 1913 the patient received another injection of 100 micrograms radium element. No blood count was made during the next three months.

In conclusion we can say that after a period of twelve days during which a slight increase and decrease of the red cells and a more marked decrease of the hemoglobin had been noted, no destructive effect upon the leucocytes could be observed. On the contrary it seems that the leucocytes were rather stimulated, resulting in a quite considerable

increase. The effect upon the erythrocytes, which were temporarily enormously increased, was most striking. Three months after another injection of 100 microgram radium element, a blood examination was made (March 16, 1914) showing that the leucocytes were still increasing to 365,000. The red cells were on the same day 3,925,000, hemoglobin 12.56 gm. (89.7%), color index 1.1. We decided therefore, to give a massive dose of radium at once, to see if a destructive effect upon the leucocytes could be accomplished. The patient received on March 16, 1914, 1,000 micrograms radium element intravenously. A blood count made two and a half hours after the injection, showed that the leucocytes were decreased from 365,000 to 260,000. The red cells were somewhat increased, while the hemoglobin was unchanged. During the next four weeks the leucocytes slowly decreased to 97,500 (April 18, 1914). A slight stimulating effect upon the red cells and hemoglobin during this period was also noted, (April 4, 1914). Increase of red cells, 697,000, hemoglobin 1.74 gm. (12.4%). The temporary decrease of the leucocytes was followed by an increase again and on May 9, 1914 the leucocytes were 182,400. On both May 9, 1914 and on May 16, 1914 he received 100 micrograms radium element. During the period of May 9th to June 13, 1914, a slight increase in the red cells was noticed, while the hemoglobin remained almost constant. The leucocytes were lowered from 220,000 to 122,400.

On June 13, 1914 the patient again received 1,000 micrograms radium element intravenously. Four days later the red cells were somewhat lowered from 4,736,000 to 4,424,000 while the hemoglobin was increased from 11.96 gm. (85.4%) to 14.36 gm. (102.6%). The leucocytes showed only a reduction from 117,600 to 109,600. The white cells were only once lowered (July 18, 1914) to 91,000, making a total reduction after the injection of 2,700,000 mache units of only 26,600. Five weeks later the leucocytes were again increasing to 240,000.

For an analysis of the changes of the leucocyte picture after injection of radium we will divide the observation time into five periods; the first period includes the time from July 1, 1913 to December 20, 1913, after 400 micrograms radium were given. The second period includes the time from December 20, 1913 to March 13, 1914, after 100 micrograms radium had been given. The third period from March 13, 1914 to May 2, 1914, after 1,000 micrograms radium were given. The fourth period from May 9, 1914 to June 6, 1914, after 200 micrograms radium were given. The fifth period from June 6, 1914 to August 29, 1914, after the second injection of 1,000 microgram radium element.

In the first period we noticed that the polynuclear neutrophiles were increased from 18.41% to 42.05%. No change was noted in the polynuclear eosinophiles, basophiles, metamyelocytes, leucoblasts, large lymphocytes, medium and microlymphocytes. The neutrophile myelocytes were reduced from 33.93% to 3.33%. The myeloblasts were increased from 4.1% to 19.33%. The large lymphocytes were decreased. The small lymphocytes were first increased and then decreased again. The monocytes disappeared entirely.

In the second period the polynuclear neutrophiles were still increased to 45.37%. The metamyelocytes and neutrophile myelocytes were decreased. The myeloblasts were markedly reduced, disappeared and increased again to 1.33%. The remainder of the leucocytes did not show any appreciable change.

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In the third period the polynuclear neutrophiles were increased to 51.37%. The polynuclear eosinophiles, basophiles and myeloblasts showed little variation. The neutrophile and eosinophile myelocytes disappeared almost entirely. The leucoblasts and the large lymphocytes were decreased. The medium lymphocytes disappeared entirely. The small lymphocytes were decreased and increased again. The micro lymphocytes and monocytes disappeared almost entirely.

In the fourth period the polynuclear neutrophiles still increased to 63.33%. The polynuclear eosinophiles and basophiles, leucoblasts, large lymphocytes and microlymphocytes showed little variation. The eosinophile myelocytes had entirely disappeared. The metamyelocytes were increased and decreased. The neutrophile myelocytes increased, the myeloblasts and the medium lymphocytes were decreased and the small lymphocytes increased.

In the fifth period the polynuclear neutrophiles decreased from 59.1% to 37.5%. The polynuclear eosinophiles, basophiles, myeloblasts, and large lymphocytes showed no appreciable change. The metamyelocytes decreased. The neutrophile myelocytes entirely disappeared and reappeared again. The eosinophile myelocytes which had entirely disappeared increased up to 1%. The small lymphocytes and microlymphocytes decreased and increased again. Monocytes disappeared and reappeared.

If we summarize the effect of the radium upon the leucocyte picture we come to the following conclusion: It seems that radium exerts a pronounced stimulating effect upon the polynuclear neutrophiles in small divided doses and in large doses. We see that during the entire period of observation the polynuclear neutrophiles were steadily increasing and once almost reached their normal number, but remained above their initial count at the end of the investigation. On the other hand we see that the eosinophile and neutrophile myelocytes, as well as monocytes are very radio sensitive, as they were markedly reduced after the small doses and disappeared after the large doses and reappeared later on in a very small percentage. The polynuclear eosinophiles, basophiles, leucoblasts, large lymphocytes, medium and micro lymphocytes seem to exhibit a variable resistance to radium.

On August 31, 1914 the patient received a cross fire radiation of 600 milligrams of radium to both femurs for three and a half hours each. The blood count taken on September 12, 1914 showed 182,000 white cells and on the 19th of September 158,000. On September 26th there were 210,000 leucocytes, 5,344,000 red cells and 14.04 gm. hemoglobin.

From September 26th to November 4, 1914 the patient received eleven X-ray treatments. A blood count on November 4th showed that the leucocytes were lowered to 167,000. Another leucocytes count taken on November 30, 1914 showed 117,600. Until the death of the patient, January 15, 1915, no other blood counts were made.

The two massive doses of 1,000 micrograms radium element each, showed a marked temporary reduction of the leucocytes, but with no reduction to the normal. The leucocytes were increased two months later to their former number. No appreciable effect was noticed during this period upon the red cells. As to the effect of the large doses of radium upon the relative leucocyte picture, the only marked influence was upon the neutrophile myelocytes and polynuclear neutrophiles.

While the myelocytes showed a continuous decrease and sometimes entirely disappeared, the polynuclear neutrophils showed a steady increase and once reached almost normal value, (63.33%) but this effect was only temporary as with the elimination of the radium the polynuclear neutrophils were decreased and myelocytes were increased again. The radiation with radium as well as the radiation with X-ray did not show any marked effect upon the leucocytes. It seems that the effect of small doses of radium given at greater intervals produced radium resistance so that further doses of radium have little or no effect upon the blood picture. It further seems that the radium resistance makes also a resistance against the X-ray as we have seen that the X-ray radiation which otherwise exerts a most powerful effect on the leucocytes had very little influence upon the radium resistant blood cells.

(To be concluded in the next number.)

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REVIEWS AND ABSTARCTS.

Frank E. Simpson, M.D. (Chicago). Radium in the Treatment of Lymphangioma Circumscriptum. Report of a Case. Journ. A. M. A., Vol. LXVI, No. 13, Mar. 25, 1916. "History.—L.L., woman, aged 21, first came under my observation at the Cook County Hospital in April, 1914. She presented a tumor of the skin involving principally the right buttock and the inner surface of the right thigh and covering an irregular surface measuring approximately 8 x 15 centimeters."

"The tumor had been present since her earliest recollection."

"It was composed principally of irregularly grouped wart-like projections more than a centimeter high at the most elevated parts and of a dirty yellowish color."

"On close inspection, the tumor was seen to be composed of innumerable thick-walled vesicles on which had developed in places a thickened hyperkeratotic epithelium giving the wart-like appearance noted before. Parts of the tumor, however, were more flat and were bluish black, being evidently made up of blood vessels. Lying beyond the main portion of the growth were many discrete, thick-walled, yellowish vesicles containing clear serum. When these were pricked a clear serous oozing took place which sometimes lasted for hours."

"From between the verrucous projections which composed the bulk of the growth a serous oozing occurred at times spontaneously, this being one of the symptoms for which relief has been sought."

"Occasionally a few new vesicles had appeared at the periphery, persisting so that a considerable increase in the size of the growth since childhood had been noticed."

"The clinical diagnosis was lymphangioma circumscriptum (lymphangiectodes, T. and C. Fox) and hemangioma. For microscopic study a small vesicle was excised, sectioned and stained with hematoxylin and eosin and with polychrome methylene blue."

"Dr. B. Barker Beeson has kindly furnished me with the following notes made from a study of the sections:

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"Microscopic Examination.—Epidermis: The stratum corneum is somewhat thickened in places but no evidences of parakeratosis are present. The granular layer is also slightly increased in size. A marked acanthosis or proliferation of the rete malpighii is a prominent feature, and, plus the hyperkeratosis, gives to the section a verrucous appearance. Throughout, the basal layer is normal."

"Corium: In the papillary and subpapillary layers one finds dilatation of the lymphatics and blood vessels, the former being especially well marked. A round-cell infiltrate surrounds the blood vessels. The number of connective tissue cells is also somewhat increased. Here and there, near the dilated lymphatics, scattered mast cells are to be seen."

"That the tumor would yield to radium was expected from the success already obtained in the treatment of many pure angiomas of the skin and from my observations of the general effects of this agent on the skin and other tissues."

"When I first undertook the treatment, in April, 1914, the effect of radium on tumors of this type had not to my knowledge been studied. Even earlier than this, however, Dr. Robert Abbe, of New York, had begun the treatment of lymphangiomas with radium, and in August, 1915, he published an account of the results obtained in four lymphangiomas of the tongue and two of the skin."

"These are apparently the first cases of this type recorded in which radium was used."

"The success following radium treatment is so striking that a brief account of the technic which I employed may be of interest."

"Treatment.—The most prominent part of the tumor was attacked first. Radium varnish applicators of one-quarter strength were usually employed. Four applicators of this type covering an area of 16 sq. cm. were applied unscreened for a period of one hour a day on four successive days. A series of four similar courses about four to six weeks apart sufficed to level the surface of the most prominent portions of the growth. As the tumor decreased in height the treatment consisted of an hourly seance each day (0.1 mm. lead screens being used over the face of the applicators) for five successive days. Two series of treatment of this sort at intervals of six weeks sufficed to cause complete retrogression of the growth."

"In the less infiltrated parts a linen 'toile' (one-twentieth strength) was sometimes used."

"With this applicator screened with 1/100 aluminium a series of applications of an hour each day on five successive days, repeated four times, at intervals of about six weeks, sufficed for decolorizing and removing these areas."

"The treatment was carried out more or less irregularly for various reasons, but the reduction of the growth, the alleviation of all symptoms and a good cosmetic appearance were obtained rather easily."

"CONCLUSION.—In view of the difficulty which is frequently experienced with other methods of treatment, the use of radium in these rare and interesting cases would seem to be the method of election."

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Richard L. Sutton, M.D. (Kansas City, Mo.) Radium in the Treatment of Synovial Lesions of the Skin. *Journ. A. M. A.*, Vol. LXVI, No. 8, pp. 565-6, Feb. 19, 1916. "It is probable that the true

nature of synovial lesions of the skin was first discovered by Sidney Jones and G. H. Makins of London, but it is to the late James Nevins Hyde that the general profession is indebted for a classical description of the disorder. In the first edition of his treatise in diseases of the skin, he states that lesions of this type—

"Occur in the form of wart-like projections from the skin, pseudo-vesicles, and bullae, always over the sites of bursae connected with tendons, traversing the small articulations of the hand and foot. They are seen over the metatarsophalangeal articulations; and in the hand most frequently over the dorsal face of the articulation between the distal and adjacent phalanges of the index finger and thumb. The first form is that of a roundish, corneous, pea-sized wart with a yellowish center, of long duration, usually insensitive unless roughly handled. When punctured there exudes a syrupy, yellowish, or grumous fluid, which continues to form after repeated puncture. Split-pea sized vesicles, and bullae as large as a 50-cent piece, often exceedingly painful, are also seen, especially on the feet, with simply an epidermic roof wall. Each lesion contains the same yellowish or whitish fluid, occasionally mingled with masses like sago grains. In every case the contents of the lesions are supplied by a synovial bursa beneath the skin, with which the lesion is either directly connected, or in communication by a short sinus."

"More recently Lingenfelter has described a typical example of the affection occurring on the dorsal aspect of the third phalangeal articulation of the second digit of the right hand, in a woman aged 51. The lesion had been present for fourteen months. Pain of a sharp, stabbing character, radiating in all directions, was present at rather frequent intervals, and was usually succeeded by a throbbing ache. In a discussion of Lingenfelter's communication, Ormsby called attention to Hyde's earlier investigations and report, and, in addition, described four cases which had come under his observation during the past eight years. Three of his patients were women, between the ages of 46 and 50, the other being a man, aged 66. The microscopic and cultural findings were negative in Ormsby's cases. He says that an arthritic diathesis is strongly suggested."

"The lesions are extremely resistant to treatment. Hyde recommended complete excision or destruction of the secreting cyst wall. Lingenfelter employed the Roentgen ray with success. Ormsby also found the use of this agent curative in two instances, although he was compelled to resort to supplemenal electrolysis in a third instance. On account of the patient's inability to remain in the city, energetic treatment was given with electrolysis, with apparent success, in his fourth case."

REPORT OF CASES.

"During the past year I have encountered two examples of the disorder."

"Case 1.—The first was in a married woman, aged 58, referred to me by Dr. C. F. Menninger of Topeka, Kan. The lesion, a smooth, rounded, pea-sized, fluctuant tumor, was located over the distal phalanx of the right index finger, and had been present eighteen months. It had been incised and drained on two different occasions, but each time the cyst had refilled, with syrupy, straw-colored fluid, as soon as the wound healed. There was intermittent pain, of a sharp, lancinating character. Treatment by electrolysis was refused because of the

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attendant discomfort, and as the patient could remain in the city for only a few hours, frequent applications of tincture of iodine, with compression by means of a small pad and bandage, were advised."

"In a recent letter, the patient says that the lesion is much reduced in size, and that the pain has disappeared. It is probable, however, that permanent relief will be secured only by the adoption of more radical remedial measures."

"Case 2.—The second case occurred in a graduate nurse, aged 26, referred to me by Dr. J. Park Neal of this city. The lesion was located over the metacarpophalangeal joint of the index finger, and had been present five months. Clinically it corresponded to the first form described by Hyde—a roundish, pea-sized, fluctuant nodule, having a depressed, yellowish center. Owing to frequent and repeated cauterization and the use of picric acid and similar agents, the surrounding skin was inflamed and eczematous. Following puncture considerable amounts of gelatinous, grumous fluid could be expressed through the opening. The patient said that the lesion varied in size at different times. When greatly distended, it gave rise to much pain and discomfort."

"Because of the encouraging reports of Lingenfelter and Ormsby following Roentgen-ray therapy, it was decided to try only radium in this case. The fractional dose method was used, a one-fourth strength applicator, unscreened, being applied for one-half hour on eight successive days. Following the subsidence of the reaction, it was found that the lesion, with the exception of a small central cicatrix, had entirely disappeared. At this time, five months having elapsed, there is no sign of recurrence. The surrounding area of dermatitis responded readily to frequent applications of calamine lotion and zinc oil."

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Walter C. Stevenson, M.D., B.Ch., D.P.H. (Dublin, Ireland). A Method of Recording Radium Doses. Illustrated by a series of eleven cases treated with one set of radium emanation capillaries in needles. Archives of Radiology and Electrotherapy. No. 186, pp. 270-276, Jan. 1916. A paper read before the Section of Surgery, Royal Academy of Medicine in Ireland, November 5th, 1915.

"It is an obvious advantage in treating patients with radium to have a uniform method of recording the dose. Only by adopting some convention in this respect can confusion be avoided, and the experience of one worker be utilized as a guide to others who are undertaking this kind of treatment."

"It is convenient to speak of the 'dose of radium,' though the therapeutic effects are not due to radium or emanation, but to the beta and gamma rays given off by their descendants, radium B and radium C, during their conversion to radium D and radium E respectively. It is immaterial therefore whether the local source of the therapeutic rays is a radium salt or radium emanation. For our purpose the difference is principally that radium is practically a constant source of therapeutic rays, while the quantity of therapeutic rays from emanation decreases at the same rate as the emanation decays. The quantity of radium is estimated by an electroscope which takes cognizance only of the rays from radium C. One millicurie of radium emanation and one milligramme of radium element are in equilibrium. They will dis-

charge an electroscope at the same rate and give off the same quantity of therapeutic rays. In both cases there is the same amount of emanation, radium A, B and C present. It is necessary to remember, however, that emanation, when it is pumped off from the parent radium and sealed in a tube, takes four hours to reach its maximum activity, that is it takes four hours for the radium C, which is in equilibrium with the emanation present, to collect. After four hours the emanation and radium C remain at equilibrium, as both decrease at what may be regarded, for practical purposes, as the same rate."

"It would be convenient, and avoid the possibility of confusion, if the quantity of therapeutic agents were at all times specified in terms of the element radium or in millicuries. Then X milligrammes of radium or X millicuries can only indicate the same definite quantity of therapeutic rays. At present this is not the case. The activity of radium or emanation is frequently given in terms of one of the radium salts. It is therefore necessary to know what standard is in use in measuring supplies from different sources. For instance, the international radium standard is Ra Cl_2 . The standard used in the Radium Institute, London, is hydrated radium bromide ($\text{Ra Br}_2 \cdot 2\text{H}_2\text{O}$). Emanation is now supplied in Dublin in millicuries, though at the time I was carrying out my investigation on the practicability of the use of radium emanation needles, the Royal Dublin Society used my radium bromide standard in estimating the dose they were good enough to supply to me for the purpose. The following quantities of radium and its salts, and the amount of emanation in equilibrium with each, have the same activity, as can be calculated from their atomic weights.

100 mg. Ra (Pure radium element).

147.4 mg. $\text{Ra Cl}_2 \cdot 2\text{H}_2\text{O}$.

131.5 mg. Ra Cl_2 .

142.5 mg. Ra SO_4 .

187.0 mg. $\text{Ra Br}_2 \cdot 2\text{H}_2\text{O}$.

170.7 mg. Ra Br_2 ."

"It is apparent, therefore, that 100 millicuries is nearly twice as active as the amount of emanation in equilibrium with 100 mg. of $\text{Ra Br}_2 \cdot 2\text{H}_2\text{O}$, the standard generally used in London."

"The dose of radium depends on the two main factors. The amount of radium in use and the length of the exposure. Turner suggests, in the *Lancet*, December 26th, 1909, that the dose should be given in milligramme-hours—the number of milligrammes multiplied by the number of hours of exposure. This term has not been generally accepted. As it stands, it is too vague and inexplicit. To begin with, the milligramme standard varies. Turner uses pure radium bromide as his. Again, two identical doses may give very different results, as if 200 mg. of radium be used for one and a quarter hours, and five milligrammes used for fifty hours, the amount of radiation would be the same, viz., 250 mgh. But the effect on the tissues would probably be very different. In this connection Lazarus Barlow has carried out a series of highly important experiments. I quote as an example from page 53, 'Archives of Middlesex Hospital,' Vol. XXXIII:—

"But the experiments show with the greatest clearness that the same arrangement of time and quantity in radium dose produces very different effects when acting upon the three types of epithelial tissues (considered as complexes). Hence, the optimum arrangement of radium dose for the treatment of a columnar cell carcinoma, with its

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attendant tissues, is different from the optimum arrangement for treating a carcinoma of a dry squamous epithelium, with its attendant tissues. The experiments show that maximal effects on the epithelial cells and minimal effects upon the associated tissues are produced in the case of a columnar cell growth, when the quantity of radium is relatively great and length of exposure of the tissue is relatively small, but is produced, in the case of a dry squamous cell growth, when the quantity of radium is smaller and the length of exposure to the rays is increased."

"However, I think there is a good deal to be said for the terms milligramme-hours or millicurie-hours. It saves circumlocution, and is quite explicit provided:—

1. The milligrammes are stated in terms of pure radium element.
2. Emanation is stated in millicuries.
3. The quantity factor and time factor are recorded in the order indicated by the term milligramme-hours.
4. The dose is registered in the form of an equation."

"Thus, when a patient received $12 \times 10 = 120$ mgh., it is clear that he had been treated by 12 mg. of Ra buried in the tissues for ten hours. If the radium is used on the surface the result is divided by 2, as at least half the rays are wasted, and the dose is recorded thus:— $12/2 \times 10 = 60$ mgh. While in a structure where the whole circumference is radiated, as in an annular cancer of the rectum, $12/1 \times 10 = 120$ mgh., explains the dose and the method. It would be an advantage also to record the amount of screening. This might be done thus, $12 \times 10 = 120$ mgh/1.5 mm. Pb, as the dose is diminished by the rays intercepted by 1.5 mm. thickness of lead."

"The term 'millicurie-hours' makes it plain that emanation is the source of radiation. The definition of a millicurie leaves no doubt as to the standard used. When using emanation, however, as its activity decreases comparatively rapidly, the quantity factor of the dose must be calculated from an emanation table. It is about the mean of the initial and final amount of emanation present. It is more accurate and usually more convenient to state the quantity as that present when half the exposure is over. It is obvious that when a dose runs into days it would be better to take the mean of the quantities present at every six or twelve hours interval. I find the millicurie-hour a particularly convenient method of recording the dose when using emanation needles—as the needles are standard bore and thickness—namely, .7 mm. in bore and 4 mm. in thickness, and the screening is always the same, .4 mm. of steel. The capillaries also are of standard capacity and length, one cubic millimeter and 1.5 centimeter respectively. Therefore, each capillary of a set will contain approximately the same quantity of emanation."

"The number of needles or foci of radiation is recorded in brackets. Thus, $12 (4) 10 = 120$ mch. indicate that four needles containing an average total of 12 millicuries, or 12 millicuries at half the period of treatment, were inserted into the tissues for ten hours, and it is obvious also that each of the four foci contained 3 millicuries. Incidentally I may mention that when using the needles the roughest outline sketch, which is made in two or three minutes, graphically shows the relative position of the needles, their distance apart, and the size, shape, and locality of the area treated. By this means, with the minimum waste of time and energy, a complete record of the dose and treatment is

secured, an essential for future reference. When sufficient, such record, accompanied by an account of the histological and clinical results of treatment are available, it will enable the question of dosage in radium therapy to be placed on a scientific basis."

"In planning the treatment to be undertaken by the use of capillaries I find it an advantage to proceed on certain lines. Cases where there is evidence to show that short exposure with a large amount of radium gives the best results, are treated first. Again, I endeavor to use fresh capillaries in such position as in the throat and mouth, where a long exposure is trying to the patient. In my experience secondary malignant glands seem to benefit most by small quantities. With the glands too the risk of over-exposure is thus lessened. Small growths, where the needles are inserted very close together, can legitimately be dealt with small quantities, and rodent ulcers are particularly benefited by long exposure with small quantities. It is usually safer to use small quantities also where a dose is being repeated."

"Besides illustrating dosage, the following account is intended to furnish an example of the amount and variety of work that can be accomplished by a single set of emanation capillaries. The cases, eleven in number, and all inoperable are not selected, but are simply those which happened to be ready for the dose of radium at the time I was able to procure it. They were treated by nine capillaries containing radium emanation which reached its maximum activity of 37.7 millicuries at 4.1 p.m. on the 4th June last, and which was supplied to me by the Royal Dublin Society Radium Institute. I may mention, one patient with malignant tonsil I had arranged to treat, died while I was waiting for it, and the second, a rodent ulcer, failed to keep his appointment."

"The series is typical of the routine I have adopted, and well illustrates the economical use of the valuable therapeutical agent. I am not at present concerning myself with the efficiency of the method, described before, and employed by me for over a year and a half, in which a number of glass capillaries containing emanation are buried in the tissues included in the lumen of fine exploring needles. Besides being extensively used in Dublin, radium emanation capillaries in needles are now, Professor Joly informs me, largely employed at the Manchester Radium Institute, which is under the direction of Professor Rutherford; and I know arrangements have been made by Dr. Russell to have them supplied at the Glasgow Radium Institute, where Mr. Fleck is in charge. Judging by the results that have been shown here, and published by others who have followed this technique, I think it may be claimed the procedure has a good deal to recommend it. It has been proved, I take it, that the method is not fraught with undue risks of over-exposure and sloughing owing to inefficient screening and secondary rays from the metal, as was suggested at the British Medical Association Meeting last year. I have already pointed out in this section that screening in radiotherapy is only a means of securing uniformity of radiation, which uniformity is secured in this method, with the minimum waste of therapeutic rays, by the sub-division of the dose into "multiple foci of illumination," as suggested by Professor Joly."

"The following is a summary of the patients treated, and contains particulars of disease, time of radiation, and dose. The dose is recorded as suggested in the beginning of this paper. For instance, 36.04 (9) 10 = 360.4 mch. indicates that the mean quantity of emanation employed or

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the amount of emanation at half-time in the treatment was 36.04 millicuries, that nine needles or foci of radiation were used, and the duration of the exposure was ten hours, while 360.4 millicurie-hours conveys an idea of the dose administered, and is a convenient record of the total amount of ionization effected."

"Summary.—Patient (1). Recurrent cancer of rectum. Time—5 p.m., 4/6/15. Dose—36.04 (9) 10 = 360.4 mch.

Patient (2). Cancer of root of tongue and epiglottis. Time—2 p.m., 5/6/15, to 1 a.m., 6/6/15. Dose—3.404 (1) 11 = 37.44 mch. Root of tongue and epiglottis. Time—1 a.m. to 10 a.m., 6/6/15. Dose—9.45 (3) 9 = 85.1 mch. Total, 112.54 mch.

Patient (3). Epithelioma palate. Time—2 p.m. to 7 p.m., 5/6/15. Dose—20.86. (6) 5 = 104.3 mch.

Patient (4). Sarcoma cheek, right nostril, and naso-pharynx. Nose. Time—2 p.m., 5/6/15, to 11 a.m., 6/6/15. Dose—6.56/1 (2) 21 = 137 mch. Naso-pharynx through palate. Time—1 a.m. to 10 a.m., 6/6/15. Dose—12/61 (4) 9 = 113.48 mch. Cheek. Time—8 p.m., 8/6/15, to 10 a.m., 9/6/15. Dose—11.23 (6) 14 = 157.5 mch. Total—407.78 mch.

Patient (5). Carcinoma ethmoidal cells, maxillary antrum and orbit. Time—1 p.m., 6/6/15, to 2 p.m., 7/6/15. Dose—24.51 (9) 25 = 612.78 mch.

Patient (6). Epithelioma vulva and glands in groin. Time—5 p.m., 7/6/15, to 8 a.m., 8/6/15. Dose—20.43 (9) 15 = 306.4 mch.

Patient (7). Malignant glands neck. Time—2 p.m., 8/6/15, to 2 p.m., 9/6/15. Dose—5.51 (3) 24 = 132.2 mch.

Patient (8). Epithelioma tongue. Time—2 p.m. to 6 p.m., 8/6/15. Dose—2.2 (6) 4 = 48.8 mch.

Patient (9). Sarcoma chin. Time—2 p.m. to 9 p.m., 9/6/15. Dose—10.06/2 (6) 7 = 35.21 mch.

Patient (10). Epithelioma of tongue with glands in neck. Time—3 p.m., 12/6/15, to 2 p.m., 13/6/15. Dose—7.35 (8) 23 = 169 mch.

Patient (11). Cancer rectum. Time—3.m., 13/6/15, to 2 p.m., 14/6/15. Dose—6.1/1 $\times$ 23 = 130.3 mch."

"Patient (1) had been operated on about a year previously for cancer of the rectum. Some nodules had developed near the anus causing partial obstruction. These nodules diminished greatly in size as a result of my treatment. The capacity of the bowel was considerably increased, and the patient was able to evacuate the rectum more freely, so that colotomy was deferred, and is still not necessary. (26th December, 1915.)"

"Patient (2) had a greatly infiltrated epiglottis which threatened to choke him. The tissue was so friable that only one needle $1\frac{1}{4}$ inches long could be made to remain in position. To overcome this difficulty I inserted needles $2\frac{1}{4}$ inches long into the root of the tongue and the epiglottis from the surface, entering them just below and in front of the angle of the jaw, and guiding them into position by the aid of my finger in the throat. The capillaries, of course, were at the point of the needles. As a result of treatment Dr. Richard Hayes verified that the tumor of the epiglottis had melted away and the whole condition of the part was very much improved. This patient had a number of glands in the neck, and was in a very critical condition when I saw him. For a time the glands became smaller and the throat improved. He died about four months later with well marked cachexia."

"Patient (3) had been treated twice previously by Dr. Murphy, of St. Vincent's Hospital, and myself. The original ulcer of the palate had completely disappeared. This treatment was undertaken for some extension along the fauces and apparently was successful in causing it to disappear."

"Patient (4) had a tumor at the junction of the upper jaw and cheek, which was about the size of a pigeon's egg, and which greatly disfigured his face. His right nostril was almost completely blocked, and two or three days previous to treatment he had had a very severe hæmorrhage from this, as a result of which he was quite blanched. His naso-pharynx was also choked up with the growth. I first put two needles loosely into his right nostril, later four right through the soft palate into growth of the naso-pharynx, and later still six needles were inserted from inside the mouth into the tumor of the cheek. This was the second dose administered in the last region. This boy has not been treated since. His nostril and naso-pharynx have become quite clear, and Dr. Richard Hayes, who kindly examined him for me, found that the growth had completely disappeared from these regions. There is still a slight swelling of the cheek. The patient considers himself well, and he looks healthy. Up to the present I have considered it unnecessary to give him further treatment. This patient, whom you have seen here to-night, was this morning examined by Dr. Hayes and myself. A swelling was found near the right Eustachian tube. This has not affected his hearing, but will require further treatment. His right nostril is perfectly clear, in fact larger than normal, as the turbinated bones have atrophied."

"Patient (5) has been operated on by Dr. Murphy, of St. Vincent's Hospital. He had considerable swelling of the right cheek over the antrum of Highmore, and proptosis of the right eye, evidently due to growth in the orbit. Six needles were inserted into the orbit, three along its inner margin, three along its lower margin, and three into the antrum through the cheek. As a result of this and a previous dose a marked depression developed over the antrum Highmore due to atrophy of the growth. The tumor of the orbit diminished, and the pain was greatly relieved. He returned to work. When I last saw the patient there were a couple of sinuses in the position where two needles had been. This patient refused further treatment, and I believe his condition has become considerably worse."

"Patient (6) had an inoperable fungating epithelioma of the vulva which caused her great pain and discomfort, and bled frequently. She was treated in April, and improved so markedly that Dr. Alfred Smith, of St. Vincent's Hospital, was easily able to remove the growth. Dr. Smith kindly wrote to me, saying, "The progress of the case was most interesting. I look forward with much concern as to the ultimate result; there is no doubt as to the clinical cure, the future can only determine its permanency. She came to my ward a physical wreck. She returned home without any trace of the tumor, feeling and looking well." The present dose was intended as a prophylactic one. I am sorry to say this patient has now, after six months, apparently some return of her trouble, and is coming up from the country for further treatment."

"Patient (7) was in a very bad way with ulcerated glands of the neck, and I do not think his condition was materially improved by the treatment on this occasion. A few months before he improved so much that he had gone back to work and neglected to attend me."

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"Patient (8) had a very chronic squamous epithelioma of the tongue, which Professor McWeeny—to whom I am much indebted for examining this and a number of other specimens—says has an extremely marked tendency to undergo keratinisation. This patient has been much improved by radium treatment. The glands under the jaw are much less evident. The mouth and tongue which were originally very foul have become clean. Treatment, especially any large dose, seems to cause the melting away of the tissue without producing a distinct slough. He has lost over half of the anterior third of his tongue."

"Patient (9) has a sarcoma of the chin which had ulcerated through the skin. The tumor had considerably diminished with previous radium treatment. The needles in this case were inserted in line into a sterilized piece of lint and used by surface application on the ulcer."

"Patient (10) appeared to derive great benefit from the treatment, but unfortunately I have since lost sight of him. When I first saw him he was hardly able to swallow fluid, a week after treatment he was able to eat meat. He stated that all the pain and soreness had gone from the root of the tongue where the disease was situated. Five needles were used in the glands; three long ones were inserted in the root of the tongue from the surface of the neck, in the same manner as in patient (2)."

"Patient (11) was an advanced case of cancer of the rectum. The treatment was employed to check the constant hæmorrhage, which it succeeded in doing to some extent. Soon afterwards he returned to the country. In this case the capillaries were fixed in the top of a thermometer case by paraffin, which was in turn surrounded by thin lead, and the whole tied in the finger of a rubber glove."

"To sum up, it will be seen that these capillaries were utilized for ten days, till their activity was reduced from 37.7 millicuries to 6.2 millicuries. Eleven patients were treated and fourteen doses were administered. The parts treated were:—the orbit, the antrum of Highmore, the nose, the naso-pharynx, the cheek, the anterior part of the tongue, the root of the tongue, the palate and fauces, the epiglottis, glands in the neck and the groin, the vagina, and the rectum. The capillaries were used in short needles and in long needles; they were buried in the tissues separately, employed for surface application, and collected into a single tube, according to the requirements of each case."

"In conclusion, I do not think an account of any work with radium in Dublin is complete without expressing the indebtedness of the medical profession in this city to the Royal Dublin Society for the arrangements they have made for supplying radium emanation for the relief of suffering in the poor as well as in the rich. We who have used the capillaries recognize how much we owe to the skill and ungrudging labour of Mr. Moss, the Registrar, who, besides being the first to make them, had to devote a great deal of time in devising and setting up the apparatus for charging them with emanation."

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Richard Weil, M.D. (New York). The Treatment of Parotid Tumors by Radium. *The Journal of Cancer Research*, Vol. 1, No. 1, p. 121-2. January, 1916. (*Proceedings of the American Association for Cancer Research*, Eighth Annual Meeting, held in St. Louis, April 1, 1915).

Full article appears in Jour. Am. Med. Assn., Vol. LXV, pp. 2138-40, December 18, 1915. "Dr. Weil reported a case of parotid tumor which had been successfully treated with radium in the Memorial Hospital of New York. A number of other favorable results with tumors of the parotid have been reported, but in no instance has the microscopic character of the tumor been described. In the present case, a small piece removed for examination was diagnosed by Dr. Ewing as adenoid cystic epithelioma. The appearance corresponds to that frequently described as cylindroma. The sections show cells resembling epithelium, and arranged in cords which have extensively infiltrated and destroyed the muscle bundles. No tissues characteristic of the "mixed tumors" were discoverable. The patient was a female aged thirty-eight. The tumor, which had been slowly growing for seven years, was seated in the parotid region and involved the entire lower half of the ear, and of the upper part of the neck behind the ear. It was firmly adherent to the deeper structures and in part to the skin. There was complete facial paralysis on the right side. The radium (10 mgm. radium bromide screened with 1 mm. lead) was inserted into the tumor through an incision, eighteen such applications being made. At the end of six weeks the tumor had practically disappeared. Up to the present time, after an interval of more than one year, there has been no evidence of recurrence. The facial paralysis, however, has not been benefited."

Discussing the above paper Dr. F. C. Wood said: "I have long been interested in this group of tumors and have seen, probably, some one hundred and twenty of them. Some years ago I examined all the specimens preserved in the laboratory of the College of Physicians and Surgeons, New York, and found that only about fifty per cent. of these had recurred, even with the imperfect operative procedures which were then employed, most of the tumors dating back twenty or thirty years."

"I think that almost all these tumors might be successfully removed, were it not for the difficulty of operating so as to avoid cutting the facial nerve. This tumor is of a type which is relatively harmless. I have followed up a number of them of similar morphology, observed in St. Luke's Hospital during the last few years, and have found no recurrence. I have seen other cases, however, which did very badly under radium treatment. The carcinomata, squamous cell epitheliomata, and sarcomata which occasionally arise in salivary gland tumors after they have existed for a good many years, are of an entirely different type, extremely malignant, and not at all susceptible to radium therapy. This case of Dr. Weil's is certainly very interesting, and illustrates the necessity for careful microscopical study of tumors before the application of radium. Growths containing cartilage are, as a rule, resistant to radium, though in general no more malignant than the basal cell epitheliomata of the face, which, as we all know, can often be treated more efficiently with radium than in any other way."

In closing Dr. Richard Weil said: "I should like to say that the tumor reported was one which cannot be accurately described as malignant, in spite of certain histological features. It invaded and infiltrated the neighboring tissues, destroyed a large part of the ear, was densely adherent, and had apparently infiltrated and destroyed the facial nerve. Yet, on the other hand, it was slowly growing and did yield to radium."

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James Ewing, M.D. (New York). *Pathological Aspects of Some Problems of Experimental Cancer Research. The Journal of Cancer Research*, Vol. 1, No. 1, pp. 83-85. January, 1916. (Read in the Symposium on Cancer Research of the Second Pan-American Scientific Congress, Washington, D. C., January 5, 1916). "On the therapeutic side, experimental cancer research still presents itself practically empty-handed. The exclusive and quite energetic pursuit of the principles of serum immunity has accomplished practically nothing, except to show that the malignant tumor process can probably not be controlled by investigations along the lines which have proven effective in bacterial diseases. Vaccination by means of tumor derivatives has been practiced on an enormous scale all over the world and has failed to justify itself. It has had some paradoxical success but has probably done more harm than good. No one has been able to improve upon Vidal's feeble showing for anticancer sera. Chemotherapy has never had any tangible basis in the tumor field, and from Weil's review it would seem to have even less claim to serious notice than has vaccination. Under these circumstances, I venture to raise the question whether it is not time to abandon this unprofitable territory and seek for help in entirely different directions. It may be the artificial alterations in the course of metabolic processes in the body, as suggested by recent dietary studies, may prove capable of influencing favorably the course of some malignant tumors. I freely confess the hope that the vegetable kingdom may be found to contain some agent that will specifically affects the cells of some tumors. It is the genius of vegetable products specifically and powerfully to affect different organs, tissues, and functions of the animal body, as exhibited by digitalis, strychnine, morphine, etc. Why should not some vegetable agent attack the delicately balanced nutrition of tumor cells? It would be extremely disconcerting, and even mortifying, if some vegetable alkaloid or glucoside were found to do more for cancer than all the theories of serum immunity, but the demonstration, if made, would have to be accepted."

"At present, the only laurels in cancer therapy are being carried off by physical agents, X-ray and radium, and it seems to be only the difficulties of accessibility and dosage which stand in the way of the successful application of these agents to all localized and some generalized tumors. Cancer research should note that progress in the development of the X-ray is almost exclusively in the hands of elaborately equipped and far sighted business corporations, from whom one department of medicine receives orders when and how to proceed. This situation is somewhat different, since the study of physics and therapeutics of radium rests with Government organizations, universities, and private institutions endowed with a supply of this precious metal. It is not too much to hope that when the early stages of cancer are recognized as a proper field for the use of X-ray and radium, as has already occurred in the opinion of some competent authorities, much of the present fear of the disease, especially of the most deplorable post-operative recurrences, will be removed. In such an event, some of the present problems of cancer research will retain only an academic interest."

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Howard A. Kelly, M.D. (Baltimore). *Some Radium Achievements. American Journal of Surgery*, Vol. XXX, pp. 73-77, 1916. "What will radium do, and what will radium not do? are two burning questions in

the medical world today, the former of which I will try to answer briefly here:"

"What radium will do in the future with increased study and experience, is a different and a more difficult question. Those of us who are using radium every day in the treatment of cancers and of sarcomata, and of fibroid tumors and of uterine hemorrhages, hope for a great extension of the field of utility in this new field of radio-therapeutics, as great it may be or even greater than the growth we have witnessed in the field of the X-ray, which at first had no known therapeutic value, but is now rendering such splendid service. Let me answer then this great question, "What is radium doing today?" Radium is useful in one way or another in almost every therapeutic field. I cannot therefore do more than set down a few of its notable achievements in the limits of a single article, giving here and there an illustration which will speak louder than any assertions I may make."

"First and foremost, let me emphasize this great fundamental fact, which applies to radium as well as to surgical operations, that is to say the earlier the case is seen the better are the results."

"We have treated over two thousand cases with radium, but, alas, many of these have only come in the very last stages of their disease, but a short distance from the end of the journey. This was due to the fact that to the popular imagination there appeared to be something magical in radium with its mysterious physical properties. Nor did it do on the other hand to send out a general warning to our professional friends to stop sending these very advanced cases, for here and there even in this group occasionally one would get well."

"Radium is not a remedy to be used all by itself. He who applies it must first of all have a broad medical experience and must be prepared to use every adjunct in making a diagnosis; let me briefly recapitulate some of our daily efforts. A careful history is followed by a careful examination of the patient from head to foot. Secretions are examined and in all cases (unless there is a special reason given to the contrary) a Wassermann test is made. Occasionally a 'cancer' is proven in this way to be a gumma and obscure nervous symptoms are cleared up. X-ray pictures are taken in all cancers of the breast and of the neck and in Hodgkin's disease and in lymphosarcomata, not to mention the systematic examination of the intestinal tract. A most careful pathological study is made of all available tissues before and after radiation."

"Let me now briefly recount some of the radium successes. I think the story cannot be too often told with thankfulness that radium cures basal-celled skin epitheliomata, especially those about the face, in over ninety per cent. of the cases when seen early. Surgery will do this too, but what shall we say to the mutilation caused by surgery when a wide excision is made, to the risk of return when the surgeon is over-eager to avoid deformity?"

"When the disease extends on to and involves the mucous membrane of the nose or mouth or when it extends back of the ear and becomes adherent to the mastoid, although there may be marked improvement, the final results are not nearly so good. Of the mastoid group we have not yet seen a single cured case."

"Cancer of the lip, if taken early, can often be eradicated; late cases are difficult to handle."

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"Where the glands of the neck are involved they ought to be removed surgically."

"Of cancer of the tongue we have had several apparent cures, but all early cases."

"In cancer of the breast the best use to make of radium is to deal with recurrences. It never replaces surgery in operable cases. Some remarkable results we have seen in utterly inoperable cases, and in large recurrent nodules fixed to the chest wall."

"Perhaps the best group of cases are the lymphosarcomata. Here radium would justify the outlay and labor involved even if it did no more than secure the remarkable results we are constantly witnessing in the disappearance of great tumor masses and in saving the lives of men in imminent danger of choking or starving to death, from the pressure of their conglomerate neck tumors."

"Out of twenty of our cases, thirteen had been operated upon and all were advanced and most of them desperate risks (with one exception) and yet we were able to give entire relief to 65%. We do not believe that surgery is justifiable any longer in this group, for here surgery is at its worst with its practically invariable recurrences and radium is at its best with its rapid dramatic cures."

"Several massive abdominal sarcomata have also shown an equally remarkable improvement."

"I would like to consider three classes of cases in the gynecological field: fibroid tumors, bleeding uteri, and cancers of the neck of the womb."

"We have treated a large series of fibroid uterine tumors with these results in general. The menstruation can be stopped in about every case, the tumor can be checked in its growth, caused to shrink and even to disappear. In young women it is often possible to preserve menstruation. Our treatment is given by simply inserting the emanation of the radium on the end of a uterine sound well within the uterus. This causes no more pain than an examination of the patient. The progressive diminution of the tumor goes on for weeks or months."

"Our position, then, regarding fibroids is this: If pressure symptoms are urgent or if there are complicating conditions such as lateral inflammation or ovarian cysts, operate. In all other cases use radium. It is astonishing how many patients we see with serious complicating conditions such as Bright's or heart disease, or diabetes which would render operation extremely hazardous or impossible. In these latter radium is, of course, supreme."

"Bleeding uteri can also always be checked and in this way a radical operation avoided. This is one of the greatest of all the boons conferred by radium."

"Now as to the great question of cancer of the cervix of the uterus. What can be done here? I give the statistics of 213 cases which Drs. Burnam, Lewis and I have seen and treated, lumping them all together."

"These 213 cases were treated with radium between January 1, 1909, and January 1, 1915. Of these cases fourteen were operable and 199 inoperable or inoperable recurrent cases."

"Of the fourteen operable cases ten patients were operated on and treated prophylactically with radium. Of these two have remained well for more than three years; one for more than two years; four for more than one year; and three for more than six months. In four cases

of the operable group, on account of some general contra-indication, to operation, radium alone was used. All of this group are living and well; two for over three years and two for over one year."

"The total number of inoperable and inoperable recurrent cases is 199, of which 53 patients have been clinically cured, 109 markedly improved and thirty-seven not improved."

"Our series includes thirty-five cases of originally inoperable cancers of the cervix uteri or vagina in which the patients are clinically cured; two cases for over three years; four cases for over two years; 17 cases for over one year; 10 cases for over six months. It also includes 18 cases of originally inoperable recurrent cancers in which the patients are now clinically cured; in one case for over six years; in one case for over four years; in eleven cases for over two years; in ten cases for over one year; in five cases for over six months."

"Excluding the ten operable cases in which we both operated and used radium, there are 203 cases left; in 57 of these 203 cases the patients are clinically cured. Of the 57 clinical cures, one has lasted for six years; three for over four years; four for over three years; five for over two years; 24 for over one year; 15 for over six months."

"Our rules, then, are:

"(1) Operate on every operable case, estimated as a good risk as heretofore"

"(2) Radiate from four to six weeks after the operation."

"(3) Do not operate on borderline cases, but use radium first, for the disease practically always returns after operation in these cases, while many are curable with radium."

"(4) Radiate all the advanced inoperable cases, for many of these too are curable, or can be shrunk down so as to become good risks."

"(5) Where there are metastases up into the abdomen, radiation may give great relief and a temporary return to apparent good health but it will not cure."

"Let me conclude by urging two things, first, that it is not enough to radiate and let the case go when apparently cured that is to say when all obvious disease is gone. All radiated cancerous cases must be kept under occasional observation for some years. A slight relapse is not infrequent and as a rule responds rapidly to another application of radium. Finally let me insist that while hoping for the great boon of a cure, we too constantly lose sight of the fact that even if radium never cured a single case it would still be one of our greatest therapeutic agents, and that it often gives such remarkable prolonged relief from pain, checks discharges, causes a cessation of foul odors and brings about a relief and general improvement with better spirits and appetite, and renewed interest in the affairs of life, a relief which is inexpressibly valuable even if it lasts only a few weeks or months."

"Radium then has come as a most potent agent to enlarge a sphere of control over the worst of all diseases. It will do many things we have never been able to do before, although it is by no means a specific, except in lympho-sarcomata."

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Francis E. Park, M.D. (Stoneham, Mass.) *The Treatment of Disease by Injections of Deep-Sea Water and Radium.* Med. Rec., Vol. 89, pp. 782-3, Apr. 29, 1916.

For a period of about fifteen years, Rene' Quinton, the originator of the treatment of disease by injections of deep-sea water, rendered

isotonic with the fluids of the body by the addition of spring water, has been carrying on in Paris his great humanitarian work. During this period he has saved thousands of lives, especially those of infants. His methods were the object of a great deal of ridicule at first, but as time wore on and the uniformly splendid results of his treatment became known, more and more respect was accorded it, until, at the time I visited him, three years ago, it was customary to find his clinic crowded by physicians from all over Europe.

My attention was drawn to this method by reading a paper written by Dr. Robert Simon of the University of Paris and published in the "International Medical Annual" of 1910. In this such strong and apparently well-substantiated claims were made, that I was induced to try the remedy in a very grave case that was under my care at that time, and with such striking results that I gave it a wide and searching trial, and now, after five years of constant use, can say unhesitatingly that nowhere in medicine, so far as my knowledge goes, have we such a potent, yet safe, general tonic.

In Quinton's book, "L'Eau de Mer, Milieu Organique," there is a very careful analysis and study of the water of the ancient ocean as revealed in deep deposits in mines. The elements revealed there are easily divided into groups. In the first, which contains in bulk more than half of all the others combined, are chlorine and sodium. In the next the amount is very small, but still present in appreciable quantities, and the minerals are sulphur, magnesium, potassium, and calcium. In the next group the amount present is exceedingly minute but still demonstrable chemically, and comprises bromine, silicon, carbon, azote, iron, iodine, manganese, phosphorus, and lithium. Then there is a fourth group, in which the presence of the elements can be determined only by means of the spectroscope; this contains boron, arsenic, copper, silver, gold, zinc, strontium, barium, cesium, rubidium, aluminum, lead, and now later investigations add to the above list, radium.

According to Quinton's researches, all of these elements, in practically the same proportions, have been demonstrated in the body fluids by competent chemists. It was this remarkable coincidence, coupled with his belief that the first living organism was found in the warm waters of the primordial ocean, that led him to the conclusion that if life originated and developed in such a medium, then the same solution applied to diseased cells, that are in structure similar to the original one, could not fail to be beneficial, by furnishing them a pabulum which they could easily assimilate, and thus regain their lost energy.

It is hardly the place here to follow the steps by which he was ultimately led to apply his theory in practice; suffice it to say that the evolution occurred, and as a result we find to-day in Paris two large clinics where this work has been carried on for many years in the most careful and scientific manner possible, with all the data for this period open for inspection. The results obtained cover such a wide variety of diseases that one is at once forced back to the very essence of things, in order to reach an adequate explanation of the effects observed, for not only do we see desperately sick enteritis cases recover in a marvelous manner, but various other conditions extending even to chronic skin lesions as psoriasis and eczema.

At the time I visited Professor Quinton, in 1913, he was holding to his original belief, that in the deep-sea water was some element of

life, which he called "marine plasma," for he had found the vital force in it was very unstable. He could neither boil the water nor keep it more than a few days without a total loss of its healing power. I suggested to him at that time my belief that he was dealing with a weak emanation of radium, but we could not agree. Within a few months, however, Professor Joly's paper appeared claiming his discovery of rich deposits of radium in the deep-sea dredgings, and his subsequent assertion of the radioactivity of the whole ocean body. Thus we had in the administration of freshly prepared solutions not only a natural food, but also the dynamic force of radioactivity to stimulate the activity of the cells and increase their power of absorption.

So much for the prologue, now for the story; what will it do?

In the first place I will state how it is prepared, and then as briefly as possible outline the conditions where it has proved of benefit.

The water is obtained out in the open ocean, in a region free from the contamination of sewage, and out of the track of vessels. I use a sterile glass bottle of a gallon capacity, and with a very small neck. This is dragged rapidly down to the depth of about 100 feet by a heavy weight attached to the rope and several feet below the bottle. It remains at that depth for fifteen minutes, and is then drawn to the surface and sealed. In my laboratory it is diluted with pure spring water in the proportion of three parts of the sea water to five of the other, and in order to make it permanently radioactive, 5 micrograms of a solution of radium barium bromide is added to every 1,000 c.c. of the mixed solution. It is then passed through a porcelain filter, and afterwards sterilized by heat. The dose varies from 10 c.c. to 200 c.c.

It can be injected with any large syringe which can be sterilized, but the best way I believe is by means of an apparatus which I have devised, patterned somewhat after that used in Paris. The accompanying illustration, I think, explains itself. It consists of (a) a glass reservoir to hold the solution, having corrugations in each of the extremities, so that the rubber tubes will not slip off; (b) a common atomizer blub which goes on the curved extremity to pump up the necessary air pressure to expel the solution; (c) the rubber tube, which slips on to the straight end and carries the needle and the brass attachment onto which the needle is screwed; (d) a small tunnel, of agate ware preferably, with a flexible rubber tube which slips onto the curved end and is used to pour the solution into the reservoir. The injection can be given in the back, sides of the abdomen, or, and this is the location of preference, in the hollow space on the thigh, just back of the greater trochanter. If the flesh is grasped tightly and held so while the 24-gauge steel needle is quickly thrust straight in, there is almost no pain. I use the same area from start to finish on a case. Of course it goes without saying that surgical asepsis should be maintained throughout.

Quinton claims, and my own experience verifies it, that the sea water is practically an absolute specific in the enteric diseases of infants. He sees the worst types of the disease brought in from the slums of the city, and by this treatment saves almost every one. I shall never forget the first case of a fatal type that I treated in this manner. A child 6 weeks of age, suffering from acute gastroenteritis, was apparently moribund at the time of my visit. I hardly expected to find it living when I got back from a hasty trip to my office to get the sea water; 200 c.c. was injected and before it was all in the child began

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to grow warm and show signs of life. The improvement was most marvelous, for an experience of over twenty years assured me that the case was hopeless. Since then I have learned always to expect a recovery in these conditions when treated in this manner.

As a general tonic after a severe sickness, I believe it is without a peer, while time and again I have been able to build up a surgical case that on account of general debility was apparently hopeless, so that in a very short time my patient was able to undergo a major operation successfully. Again I use it as a routine practice in the convalescence following all my severe surgical work, and am sure that I derive great benefit from it. In simple anemia and chlorosis, and as an adjunct to thorium X in the treatment of the pernicious type it is of proved worth.

In various skin affections, especially psoriasis and chronic eczema, Quinton has done some very remarkable work, and has a collection of photographs of cured cases that cannot be duplicated. My own experience in this line has been small, but my results have been equally striking.

In elderly patients the effect of the treatment is very gratifying; in fact, they seem to respond a good deal as do the children, and were it not for taking up too much space I could narrate some very interesting illustrative cases.

Another class of disease where I employ it as a most satisfactory routine treatment, is neurasthenia, and every medical man can test this very nicely in his own experience. There are always times in our busy life when the work comes so fast that we are tired out, and it is hard to keep going. This is the condition that has steered so many of our profession into the use of alcoholic stimulants and drugs. The effect of the solution in this condition is simply magical, as I can testify from many personal experiences. In my own case I pass, in about twelve hours, from a condition of exhaustion, to one of perfect well being, and this condition persists.

As for contraindications, I know of none. In the five years that I have employed it, and I use it very largely, I have never seen the slightest harm come from its use, barring a small number of abscesses in the early days, that were directly traced to a septic needle.

In conclusion, I believe that the medical world owes a debt of gratitude to Prof. Rene' Quinton which as yet it but little realizes, but some day will to the uttermost, as the treatment becomes more generally known.

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F. J. Schoenenberger and S. William Schapira (New York). Application of Radium in the Bladder for Carcinoma, with Report of two cases. *Journ. Am. Med. Assn.* LXIII, pp. 1852-3. Nov. 21, 1914.

To review at this time the various surgical conditions to which radium has been applied would be without gain, in view of the very recent development of our knowledge and use of this new element, which is being brought to our attention almost daily. We believe, however, that in reporting our cases, we are presenting for the first time a complete history of the action of radium as applied in the bladder in cases of carcinoma, accompanied as they are by cystoscopic examinations before and after application, microscopic examinations of the tumors and end-results.

After a careful review of the literature we find very few cases in which radium was applied in the bladder in cases of carcinoma. One case is reported by Cauhape in which he applied radium to the bladder for carcinoma of the prostate with cure in nine months. These applications were made with radium attached to a catheter and introduced into the bladder per urethram. Twenty-five mg. of radium were used and the applications made every three days, each application lasting two hours. Wickham and Degrais in their latest work do not mention the use of radium in the bladder. The Radium Institute of London in 1912 reported two patients treated with results not noted, and also two patients for prophylactic treatment, reported as improving. The Royal Infirmary of Edinburgh reported no bladder cases in 1912. The foregoing constitutes about all the information that we could obtain, demonstrating that in only one authenticated case, (that of Cauhape) is there any definite report as to the nature of the tumor, amount of radium used, length of application and end-result.

The two cases that have come under our observation are as follows:

Case 1. M. J. T., aged 34, consulted us, September 23, 1913. Family history shows that father probably died of carcinoma of stomach. Patient gives history of hematuria for about five years, occurring at intervals of about three months until recently, when attacks became very much more frequent. There had been no pain until shortly before the patient's visit to us. At this time the patient complained of hematuria and sharp pains in right inguinal region radiating to pelvis. Examination showed patient to be in fair physical condition. There was a left bubonocoele. In right inguinal region a mass about the size of an orange could be felt. This mass was hard, immovable and extended down into the pelvis. There was edema of the right thigh. Cystoscopy showed a tumor, about the size of an English walnut, situated in the trigon, midway between its center and the opening of the left ureter in the bladder. The tumor was friable. The right ureter was obstructed, but showed urine escaping. Examination of metastatic growth, microscopically, showed the tumor to be carcinoma.

October 7, 1913, a suprapubic cystotomy was done. A tube containing 15 mg. of radium was attached to the lower end of a Freyer tube and introduced into the bladder in direct contact with the tumor and allowed to remain in place for twelve hours. No discomfort was complained of by the patient at any time during the application. The same tube of radium after removal from the bladder was buried in an incision over the metastatic growth and allowed to remain in place for twelve hours. The bladder wound was completely closed on the eleventh day after the operation. Recovery from the operation was uneventful except for unaccountable attacks of pyrexia, beginning forty-eight hours after operation, lasting for three days and recurring again at the end of a week. Three such attacks occurred. Cystoscopy, December 8, two months after operation, showed that the tumor of the bladder had entirely disappeared. The mucous membrane of the bladder appeared normal. Both ureteral openings were obstructed. The metastatic tumor in the groin was about the size of an English walnut. The patient died six months after operation from general asthenia and hydronephrosis due to obstruction of ureters by metastatic growths in the pelvis.

Case 2. B. K., aged 67, was first seen by us January 4, 1914. Family history was negative. Patient complained of frequency of

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urination day and night for about eighteen months. During the last three months he has had pain in the region of the bladder and perineum accompanied by frequency and hematuria. He has lost about 40 pounds in the last three months. His appearance is cachectic. He was discharged from the German Hospital, after ten days' observation, as having an inoperable case. Residual urine was 12 ounces, bloody and ammoniacal. Blood-pressure from 190 to 170. Blood examination: White cells, 18,000; polynuclears, 83 per cent.; lymphocytes 11 per cent.; eosinophils, 1 per cent. Rectal examination shows large hard prostatic tumor. Cystoscopy shows large bleeding tumor slightly to left of left ureteral opening; smaller tumor near the right ureteral opening; also large eroded and bleeding tumor at site of prostate. The entire mucous membrane of the bladder appears infiltrated. Diagnosis: Carcinoma of prostate and bladder.

Patient entered hospital January 6, and a permanent catheter was introduced for drainage and irrigation preparatory to operation, suprapubic cystotomy, which was performed January 8. A tumor the size of an egg at the site of the left ureteral opening was removed. A tumor on the right side, somewhat smaller, was also removed. A V-shaped section was removed from the prostatic tumor. The prostatic growth is considered by us to have been the primary focus in this case. The section taken from the prostate also provided better drainage through the urethra. The same procedure in the use of the radium was pursued as in Case 1. The bladder was closed in three weeks. The same unaccountable pyrexia occurred as in Case 1. Patient was discharged from the hospital February 5, about four weeks after operation. At this time the patient was passing clear urine four times a day and every three hours at night at our direction to prevent distention of bladder and reopening of suprapubic wound. Patient gained 26 pounds in weight in two months. Cystoscopy, April 22, showed bladder mucosa apparently normal, the surfaces from which tumors had been removed appearing as small pale, depressed areas. All of the surfaces appeared to be covered by normal mucous membrane. Rectal examination showed prostate greatly diminished in size and of normal consistency. Residual urine, 3 ounces.

The pathologic report of Case 1 is from the laboratory of St Francis Hospital; the pathologic report of Case 2, is from the laboratory of the City Hospital.

CONCLUSIONS: 1. We may without danger, even without discomfort to the patient, place in the bladder as much as 15 mg. of radium and allow it to remain as long as twelve hours.

2. We believe that we have shown that radium has the power to remove a tumor of the bladder (carcinoma) and of the prostate within a period of two months. It has also been demonstrated in Case 1 that radium has had a very decided effect in reducing the size of a metastatic growth associated with carcinoma of the bladder.

3. No difference seems to have been evident in the result whether or not part of the tumor was removed. In Case 1 no part of the tumor was removed, while in Case 2 a considerable portion of the tumors was excised.

4. We are of the opinion that the peculiar pyrexia associated in both cases was due to an absorption following the destructive influence of the radium on the tumors. A thorough investigation did not disclose any other cause.

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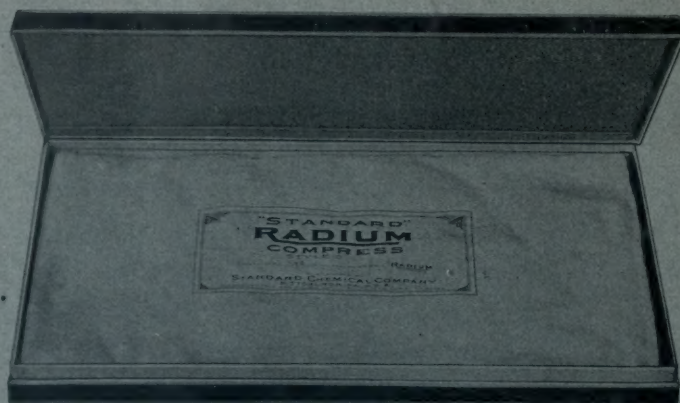
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